

What is claimed is:

1. A method of preventing, reducing and reversing the toxic effects of anti-inflammatory drugs and enhance their beneficial effects, comprising administering to a subject an effective amount of deprenyl or propargylamine compounds (monoamine oxidase [MAO] inhibitors). The anti-inflammatory drug and MAO inhibitor can be chemically linked, physically mixed or administered separately.
2. A method according to claim 1, wherein said antiinflammatory drug is selected from a group consisting of nonsteroidal antiinflammatory drugs (NSAIDS) , steroids, acetaminophen (COX-3 inhibitors), 5- lipoxygenase inhibitors, leukotriene receptor antagonists, leukotriene A4 hydrolase inhibitors, angiotensin converting enzyme antagonists, antihistaminics, histamine 2 receptor antagonists, phosphodiesterase-4 antagonists, cytokine antagonists, CD44 antagonists, antineoplastic agents, 3-hydroxy-3-methylglutaryl coenzyme A inhibitors (statins) , alpha blockers, beta blockers, estrogens, androgens, antiplatelet agents, antidepressants, Helicobacter pylori inhibitors, proton pump inhibitors, thiazolidinediones, dual-action compounds, combinations of these drugs with other agents, derivatives and metabolites of synthetic and natural antiinflammatory agents.
3. A method according to claim 1. wherein said NSAID is selected from a group consisting of nonspecific cyclooxygenase inhibitor, COX-1 inhibitor, COX-2 inhibitor, as well as metabolites and derivatives thereof.
4. A method according to claim 1, wherein said deprenyl or propargylamine compound is selected from the group of MAO-A and MAO-B inhibitors consisting of l-deprenyl [R-(-)deprenyl or selegiline], d-deprenyl [S-(+)-deprenyl], acetylenic tryptamine derivatives ,clorgyline, pargyline,

iproniazid, nialamide, phenelzine, tranylcypromine, quinacrine, hydrazine, carboxamide, RO 16-6491 [N-(2-Aminoethyl-chlorobenzamide)], RO 41-1049 [N-(2-aminoethyl-5-3fluorophenyl thiazolecarboxamide)] , propargylamines (e.g.; lazabemide, rasagiline), N-propargylamine compounds (N-methyl propargylamine and N-methyl-N-(2 pentyl)-propargylamine), and derivatives and metabolites there of including MAO inhibitors from synthetic or natural sources.

5. A method according to claim 1, wherein the antiinflammatory drug toxicity is ameliorated by the cytoprotective actions of MAO inhibitors comprising of MAO inhibition, neuroprotection, endothelial protection , antiinflammatory action, antiplatelet action, antiatherogenic action, inhibition of activation and migration of leukocytes, decreasing the levels inflammatory markers, antioxidant action, free radical scavenging, antiapoptotic action, reduction of hypoxia, reduction of oxidative stress, antagonism of cytotoxic actions of toxic agents such as amyloid- β peptide, inhibition of tumor growth, vasodilation, increased blood flow, enhanced expression of antioxidant enzymes and growth factors, stimulation of constitutive nitric oxide synthase enzymes resulting in the enhanced production of nitric oxide, and inhibition of cytochrome P450 enzymes.
6. A composition comprising of the compound claim 1 and a pharmaceutically acceptable carrier.
7. A method according to claim 1, wherein the MAO inhibitor treats, prevents, decreases or reverses the toxic side effects of antiinflammatory drugs consisting of gastrointestinal toxicity, renal damage, liver damage and platelet dysfunction.
8. A method according to claim 6, wherein the MAO inhibitor treats, prevents, decreases or reverses gastrointestinal disorder consisting of inflammatory bowel disease, Crohn's disease, gastritis, irritable bowel syndrome, ulcerative colitis,

peptic ulcer, stress ulcer, bleeding ulcer, dyspepsia, gastroparesis, Zollinger-Ellison syndrome, gastroesophageal reflux disease, or Helicobacter pylori infection.

9. A method according to claim 6, wherein MAO inhibitor prevents or treats gastrointestinal ulcers and provides tissue protection when administered alone or in combination with other agents (histamine-2 receptor antagonists, proton pump inhibitors, mucosal protective agents or prostaglandins) used in the treatment of ulcers.
10. A method according to claim 6, wherein MAO inhibitor ameliorates the toxic side effects of low dose aspirin and other NSAIDS, wherein these drugs are used for the prevention of disorders and their complications consisting of cardiovascular disease, diabetes, stroke, dementia and cancer.
11. A method according to claim 6, wherein the MAO inhibitor prevents, decreases or reverses the toxic gastrointestinal effects of NSAIDS consisting of dyspeptic symptoms, gastric and duodenal ulcers, intestinal bleeding, perforation of gastro-duodenal mucosa and gastric outlet obstruction.
12. A method according to claim 6, wherein the MAO inhibitor prevents, decreases or reverses the toxic renal effects of antiinflammatory drugs and provides cytoprotection when administered alone or in combination with other drugs.
13. A method according to claim 6, wherein the MAO inhibitor prevents, decreases or reverses disorders resulting from elevated levels or activities of proinflammatoy enzymes consisting of COX-1, COX-2, COX-3, lipoxygenase, phosphodiesterase, angiotensin converting enzyme, or leukotriene A4 hydrolase.

14. A method according to claim 12, wherein the disorder resulting from elevated levels or activities of proinflammatory enzymes are arthritis, asthma, allergy, angiogenesis, tendonitis, inflammatory muscle disease, bursitis, polycythemia vera, neoplasia, inflammatory bowel disease, pulmonary inflammation, cardiovascular disease, atherosclerosis, stroke, diabetes, bacterial or viral infection, septic shock, urinary or urological disorder, endothelial dysfunction, platelet aggregation, leukocyte activation, reperfusion injury, stent obstruction, neuronal dysfunction, or central nervous system disorders.
15. A method according to claim 14, wherein neoplasia resulting from elevated levels or activities of proinflammatory enzymes are gastrointestinal cancer, bone cancer, brain cancer, epithelial carcinoma, basal cell carcinoma, adenocarcinoma, esophageal cancer, stomach cancer, colon cancer, liver cancer, pancreas cancer, bladder cancer, prostate cancer, renal cell carcinoma, lung cancer, ovarian cancer, cervical cancer, breast cancer, polyp, adenomatous polyp, familial adenomatous polyposis, fibrosis, or cancers caused by radiation therapy.
16. A method according to claim 14, wherein the central nervous system disorder resulting from elevated levels or activities of proinflammatory enzymes are Alzheimer's disease, vascular dementia, cortical dementias, multi-infarct dementia, pre-senile dementia, mild cognitive impairment, senile dementia, Down's syndrome, amyloid angiopathy, amyloidosis, prkinson's disease, depression, anxiety, or brain damage resulting from stroke, ischemia or trauma.
17. A method according to claim 6, wherein the MAO inhibitor prevents or treats the toxic side effects of NSAIDS and provides tissue protection when administered as a separate compound or the MAO inhibitor is chemically linked to the NSAID

18. A method according to claim 6, wherein the MAO inhibitor preserves and enhances the anti-platelet, cardiovascular or anticancer benefits of aspirin and reduces aspirin resistance when aspirin is administered alone or in combination with other NSAIDS.
19. The pharmaceutical composition of claim 6, wherein the therapeutically effective amount of MAO inhibitor in a pharmaceutical composition is in the amounts of 0.1 to 10 times the molar equivalent of the NSAID. The usual daily doses of NSAIDS are 1-40 mg / kg body weight and the doses of MAO inhibitors in the pharmaceutical composition may be in the amounts of 0.1-500 mg / kg body weight daily and more usually about 0.1-50 mg / kg..
20. A method according to claim 17, wherein the MAO inhibitors can be linked to NSAIDS by various methods, for example a NSAID can be covalently linked to a MAO inhibitor of the propargylamine type having the general formula (1) to form an amide bond :



Where R is a hydrogen , alkyl $[CH_3 CH_2]_n$ and n is an integer from 1-20, aryl, alkyl aryl group or alkoxy or aryloxy group and salts thereof and other monoamnine oxidase (MAO A and B) inhibitors containing a propargyl group. In cases where the MAO inhibitors do not have a free amino group available, as in the case of deprenyl, clorgyline or pargyline, a free amino group is introduced at the propyl carbon by arts known in the literature. The NSAID can be selected from a group of compounds containing a free carboxyl group (-COOH) such as aspirin, genistic acid, indomethacin, ibuprofen, ketoprofen, flubiprofen, diclofenac, meclofenamic acid, fenoprofen, oxaprocin, etodolac, and other NSAIDS to which a -COOH group can be attached. Different MAO inhibitors and derivatives thereof can be attached to different NSAIDS by other methods known in the literature.

21. A method of treating gastrointestinal ulcers due to causes other than NSAIDS, comprising administering to a subject suffering from such disorder an effective amount of a MAO inhibitor alone or in combination with agents used in the treatment of such ulcers.
22. A method according to claim 21, wherein the ulcer is a stress-induced ulcer and MAO inhibitor is selected from a group comprising of MAO-A or MAO-B inhibitors.
23. A method according to claim 21, wherein the ulcer is a helicobacter pylori, alcohol, tobacco, or drug induced ulcer and the MAO inhibitor is selected from a group comprising of MAO-A or MAO-B inhibitors.
24. A method for treating inflammation, pain, or fever in an animal in need thereof comprising administering the composition of claim 6 to treat inflammation, pain or fever.
25. A method of preventing or treating side effects of COX 2 inhibitors such as gastrointestinal damage, mucosal damage , endothelial dysfunction, and cardiovascular disease, edema, hypertension, renal damage and also provide additional cardiovascular protection by administering to the animal in need thereof a therapeutically effective amount of the composition of claim 6.
26. A method for accelerating gastrointestinal and other tissue repair in an animal in need thereof comprising administering to the animal a therapeutically effective amount of the composition of claim 6.
27. A method of treating arthritis, pain, inflammation, vascular disease and cognitive dysfunction syndrome (dementia) in dogs , cats and other animals by

administering to the animal a therapeutically effective amount of the composition of claim 6.

28. A method of preventing NSAID toxicity and providing tissue protection by administering a therapeutically effective amount of the composition of claim 6, when the NSAID is administered along with other drugs for the treatment of a number of conditions (e.g. NSAID administered with estrogens, acetyl cholinesterase inhibitors, NMDA receptor antagonists, statins, secretase inhibitors, or amyloid vaccines for the treatment of Alzheimer's disease; or aspirin administered with antihypertensives, antiplatelet drugs, estrogens, antioxidants, angiotensin converting enzyme(ACE) inhibitors, ACE receptor antagonists, or statins for the treatment of cardiovascular disease).
29. A method of providing protection to tissues such as blood vessels, heart and the brain in an animal treated with a therapeutically effective amount of the composition of claim 6.
30. A method for preventing or treating diseases caused by increased production, aggregation or deposition of amyloidogenic proteins (e.g. amyloid-beta, prions, amylin, alpha-synuclein, tau, huntingtin, polyglutamate, amyloidogenic proteins etc.) in animal by administering to the animal a therapeutically effective amount of the composition of claim 6.
31. A method for treating an inflammatory disorder (cardiovascular disease, diabetes, Cancer or Alzheimer's disease) or adverse effects of hormone replacement therapy by reducing the levels of inflammatory mediators (like cytokines ,C-reactive protein, and myeloperoxidse) in an animal in need thereof comprising

administering to the animal a therapeutically effective amount of the composition of claim 6.

32. A method for treating an inflammatory disease state or disorder in an animal in need thereof comprising administering to the animal a therapeutically effective amount of the composition of claim 6.

33. The method of claim 32, wherein the inflammatory disease state or disorder is a reperfusion injury to an ischemic organ, inflammatory bowel disease, Krohn's disease, irritable bowel syndrome, rheumatoid arthritis, osteoarthritis, gout, gum and dental inflammation and pain, acne, inflammatory skin diseases, skin wrinkles, allergic and airway inflammation, peripheral neuropathy hypertension, eclampsia, chronic renal failure, kidney disease, hepatitis, organ transplant rejections, organ preservation, radiation-induced injury, cancer, asthma, atherosclerosis, thrombosis, platelet disorders, stroke, burns, head trauma, spinal trauma, post surgical or trauma pain, pancreatitis, diabetes, disseminated intravascular coagulation, thromboembolism, Alzheimer's disease (inherited or sporadic), vascular dementia, amyloid angiopathy, Down's syndrome, attention deficit disorder, fibromyalgia, macular degeneration, multiple sclerosis, amyotrophic lateral sclerosis, encephalitis, epilepsy, amyloidosis, and cognitive dysfunction syndrome in cats and dogs.

34. A method for preventing and treating antiinflammatory drug discontinuation disorder in an animal in need thereof comprising administering to the animal a therapeutically effective amount of the composition of claim 6.